

## § 486.318

(e) A hospital may request and HCFA may grant a waiver permitting the hospital to have an agreement with a designated OPO other than the OPO designated for the service area in which the hospital is located. To qualify for a waiver, the hospital must submit data to HCFA establishing that—

(1) The waiver is expected to increase organ donations; and

(2) The waiver will ensure equitable treatment of patients referred for transplants within the service area served by the hospital's designated OPO and within the service area served by the OPO with which the hospital seeks to enter into an agreement.

(f) In making a determination on waiver requests, HCFA considers:

(1) Cost effectiveness;

(2) Improvements in quality;

(3) Changes in a hospital's designated OPO due to changes in the metropolitan service area designations, if applicable; and

(4) The length and continuity of a hospital's relationship with an OPO other than the hospital's designated OPO.

(g) A hospital may continue to operate under its existing agreement with an out-of-area OPO while HCFA is processing the waiver request. If a waiver request is denied, a hospital must enter into an agreement with the designated OPO within 30 days of notification of the final determination.

[59 FR 46517, Sept. 8, 1994. Redesignated and amended at 60 FR 50447, 50448, Sept. 29, 1995; 61 FR 19745, May 2, 1996]

## § 486.318 Changes in ownership or service area.

(a) *OPO requirements.* (1) A designated OPO considering a change in ownership or in its service area must notify HCFA before putting it into effect. This notification is required to ensure that the entity, as changed, will continue to satisfy Medicare and Medicaid requirements. A change in ownership takes place if there is the merger of one entity into another or the consolidation of one entity with another.

(2) A designated OPO considering a change in its service area must obtain prior HCFA approval. In the case of a service area change that results from a change of ownership due to merger or

## 42 CFR Ch. IV (10–1–99 Edition)

consolidation, the entities must submit anew the information required in an application for designation, or other written documentation HCFA determines to be necessary for designation.

(b) *HCFA requirements.* (1) If HCFA finds that the entity has changed to such an extent that it no longer satisfies the prerequisites for OPO designation, HCFA may terminate the OPO's agreement and declare the OPO's service area to be an open area.

(2) If HCFA finds that the changed entity continues to satisfy the prerequisites for OPO designation, the period of designation of the changed entity is the remaining designation term of the OPO that was reorganized. If more than one designated OPO is involved in the reorganization, the remaining designation term is ordinarily the longest of the remaining periods. HCFA may determine, however, that a shorter period applies if it decides that a shorter period is in the best interest of the Medicare and Medicaid programs. The performance standards of § 486.310 apply at the end of this remaining period.

[59 FR 46517, Sept. 8, 1994. Redesignated and amended at 60 FR 50447, 50448, Sept. 29, 1995]

## § 486.325 Terminations of agreement with HCFA.

(a) *Types*—(1) *Voluntary termination.* If an OPO wishes to terminate its agreement, it must send written notice of its intention with the proposed effective date to HCFA. HCFA may approve the proposed date, set a different date no later than 6 months after the proposed effective date, or set a date less than 6 months after the proposed date if it determines that it would not disrupt services to the service area or otherwise interfere with the effective and efficient administration of the Medicare and Medicaid programs. If HCFA determines that a designated OPO has ceased to furnish organ procurement services to its service area, the cessation of services is deemed to constitute a voluntary termination by the OPO, effective on a date determined by HCFA.

(2) *Involuntary termination.* HCFA may terminate an agreement if it finds that an OPO no longer meets the conditions for coverage in this subpart, or is

not in substantial compliance with any other applicable Federal regulations or provisions of titles XI, XVIII, or title XIX of the Act. HCFA may also terminate an agreement immediately in cases of urgent need, such as the discovery of unsound medical practices.

(b) *Notice to OPO.* HCFA gives notice of termination to an OPO at least 90 days before the effective date stated in the notice.

(c) *Appeal right.* The OPO may appeal the termination in accordance with the provisions set forth in part 498, which sets forth appeals procedures for determinations that affect participation in the Medicare and Medicaid programs.

(d) *Effects of termination.* When an OPO agreement is terminated—

(1) Medicare and Medicaid payments may not be made for organ procurement services the OPO furnishes on or after the effective date of termination; and

(2) HCFA will accept applications from any entity to be the designated OPO for that area.

(e) *Public notice.* In the case of voluntary termination, the OPO must give prompt public notice of the date of termination, and such information regarding the effect of that termination as HCFA may require, through publication in local newspapers in the service area. In the case of involuntary termination, HCFA gives notice of the date of termination.

(f) *Reinstatement.* HCFA may, at its discretion, designate an OPO whose agreement was previously terminated if HCFA finds that the cause for termination has been removed, is satisfied that it is not likely to recur, has not designated another OPO for the service area, and finds that the OPO meets all the necessary requirements for designation.

[59 FR 46517, Sept. 8, 1994. Redesignated and amended at 60 FR 50447, 50448, Sept. 29, 1995; 61 FR 19745, May 2, 1996]

## APPENDIX A TO SUBPART G OF PART 486

## **Guidelines for Preventing Transmission of Human Immunodeficiency Virus Through Transplantation of Human Tissue and Organs**

### **Summary**

*Although previous recommendations for preventing transmission of human immunodeficiency virus (HIV) through transplantation of human tissue and organs have markedly reduced the risk for this type of transmission, a case of HIV transmission from a screened, antibody-negative donor to several recipients raised questions about the need for additional federal oversight of transplantation of organs and tissues. A working group formed by the Public Health Service (PHS) in 1991 to address these issues concluded that further recommendations should be made to reduce the already low risk of HIV transmission by transplantation of organs and tissues. In revising these recommendations, the PHS sought assistance from public and private health professionals and representatives of transplant, public health, and other organizations. The revised guidelines address issues such as donor screening, testing, and exclusionary criteria; quarantine of tissue from living donors; inactivation or elimination of infectious organisms in organs and tissues before transplantation; timely detection, reporting, and tracking of potentially infected tissues, organs, and recipients; and recall of stored tissues from donors found after donation to have been infected. Factors considered in the development of these guidelines include differences between the screening of living and cadaveric donors; time constraints due to organ/tissue viability that may preclude performing certain screening procedures; differences in the risk of HIV transmission from various organs and tissues; differences between systems for procuring and distributing organs and tissues; the effect of screening practices on the limited availability of organs and some tissues; and the benefit of the transplant to the recipient.*

### **INTRODUCTION**

Exclusion of prospective blood donors based on their acknowledged risk behaviors for human immunodeficiency virus (HIV) infection began in 1983 (1). In 1985, when tests for HIV antibody became available, screening prospective donors of blood, organs, and other tissues also began (2,3). Both measures have reduced markedly the transmission of HIV via these routes.

A 1991 investigation determined that several recipients had been infected with HIV by an organ/tissue donor who had tested negative for HIV antibody at the time of donation (4). This occurrence raised questions about the need for additional federal oversight of transplantation of organs and tissues. To address these questions, the Public Health Service (PHS) formed a working group comprising representatives from several federal agencies. The working group concluded that, although existing recommendations are largely sufficient, revisions should be made to reduce the already low risk of HIV transmission via transplantation of organs and tissues. Adequate federal

regulations, recommendations, and guidelines for blood and plasma are already established and are not addressed in this document.

Those developing guidelines for other organs and tissues should consider donor screening and testing; quarantine of tissue from living donors; inactivation or elimination of infectious organisms in organs and tissues before transplantation; timely detection, reporting, and tracking of potentially infected organs, tissues, and recipients; and recall of stored tissue from donors found after donation to have been infected.

These guidelines apply largely to donation and transplantation of organs and solid tissues. Although they also apply generally to donation of human milk and semen, some modifications may be needed because donors of human milk and semen are living and often donate repeatedly. Additionally, donor milk should be pasteurized (a heating procedure that inactivates HIV) before dispensing. This document can serve as a general guide to facilities that bank breast milk or semen and should be followed where feasible.

In revising these recommendations for transplantation of organs and tissues, PHS sought assistance from public and private health professionals and representatives of transplant, public health, and other organizations (see pages iii-v). These guidelines do not supersede existing state laws but are to be implemented in accordance with existing statutes.

## **BACKGROUND**

### **Epidemiology of HIV Infection in Recipients of Organs and Tissues**

Most transmission of HIV to organ/tissue recipients occurred before 1985, before the implementation of donor screening. In addition to HIV transmission through blood and blood products, reports of HIV infection following transplantation have implicated the kidney, liver, heart, pancreas, bone, and possibly skin as sources of infection (4). HIV has also been transmitted from infected semen during artificial insemination (5). Several studies and case reports indicate that HIV can be transmitted through breast milk from HIV-infected women to their children (6,7); these investigations include several prospective studies indicating that breast-fed infants are at greater risk of acquiring HIV from their infected mothers than are bottle-fed infants (8,9).

Reports of transmission from screened, HIV-antibody-negative donors of organs or tissues have been rare. In one instance, hemodilution from multiple transfusions given to the organ/tissue donor before collection of the blood sample resulted in an HIV-antibody test result that was initially false negative (10). Serum samples taken on admission, before the transfusions, and 2 days after the transfusions later tested positive for antibody to HIV. In another instance, a kidney donor tested HIV-antibody negative 8 months before donation but seroconverted between the time of testing and donation (11). The donor was not retested at the time of donation. In a third instance, an organ from an HIV-infected donor was transplanted under emergency conditions before results of the HIV-antibody test were known (12).

A fourth case involved transmission from an organ/tissue donor whose HIV-antibody test was negative at the time of donation (4). Most likely, the donation occurred sometime between infection and antibody seroconversion, which, for most

infected persons, ranges from 4 weeks to 6 months (13). Six years after the donor's death and ensuing donation, HIV infection in the stored donor material was confirmed by virus culture and polymerase chain reaction (PCR) of stored donor lymphocytes (4). Among the 41 recipients identified and tested, those who received the solid organs and unprocessed, fresh-frozen bone acquired HIV infection from the allografts (one recipient of a heart, two recipients of kidneys, one recipient of a liver, and three recipients of fresh-frozen bone). The recipients of other processed bone and relatively avascular soft tissue (fascia lata, tendons, ligaments, dura mater, and corneas) did not become HIV infected (4).

#### **Current Use of Organ and Tissue Transplants**

The number of transplants has grown considerably over the last several years, a phenomenon attributable to many factors, including the availability of improved immunosuppressant drugs. Approximately 66 Organ Procurement Organizations (OPOs) and 260 organ transplant centers are members of the Organ Procurement and Transplantation Network (OPTN). In 1990 these centers recovered approximately 15,000 organs (e.g., kidney, liver, heart, lung, and pancreas) from 4,500 donors.

OPOs and tissue banks also recovered tissues (other than the organs listed above) from an estimated 7,500–10,000 donors in 1990. These tissues were used in approximately 250,000–300,000 (mostly bone) allografts.

In 1990, member banks of the Eye Bank Association of America (EBAA) retrieved ocular tissue from more than 40,000 donors. These tissues are used for corneal transplantation and are also processed into epikeratophakia lenticules (EBAA Statistical Report, 1990).

More than 400 establishments either bank or commercially process one or more human tissues. Approximately 100 eye banks and 125 bone banks operate in the United States (although the number of hospitals that store bone for future transplantation is difficult to estimate). Also, several hospitals may retrieve and store bone from living donors. Seven human milk banks operating in the United States process donor breast milk.

The American Fertility Society is aware of approximately 100 semen banks in the United States. Slightly fewer than half of artificial inseminations performed in the United States involve unrelated-donor semen used to inseminate approximately 75,000 women per year. In addition to these 100 semen banks, an undetermined number of smaller banks are hospital based or located in the offices of individual physicians.

The National Heart, Lung, and Blood Institute (NHLBI) within the National Institutes of Health (NIH) is aware of 99 bone marrow transplant centers, of which 41 participate in programs involving bone marrow transplants from unrelated donors. Many additional facilities are equipped to obtain marrow from donors. About 2,200 bone marrow transplants involving allogeneic marrow took place in the United States in 1991. Of those, approximately 435 were provided by donors who were not related to the recipients. Peripheral blood stem cells are being used for autologous transplantation and, in the future, may be useful for allogeneic use. Furthermore, cord blood stem cells are being used for both related- and unrelated-donor allogeneic transplantation.

**Current Guidelines and Recommendations**

Procedures for procurement and transplantation of organs and tissues are addressed by a) federal laws, regulations, and guidelines; b) state laws and regulations; and c) voluntary industry standards. Several federal agencies either directly or indirectly regulate procurement and transplantation of organs and tissues. These activities range from the publication of guidelines that address the transmission of communicable diseases through transplantation to regulatory requirements for registration and premarket product licensure or approval (blood and certain other tissue products).

The Health Resources and Services Administration (HRSA), through the United Network for Organ Sharing (UNOS), administers the contract for OPTN as required by Section 372 of the Public Health Service Act and as amended [42 USC 274]. The contract covers specified solid organs (kidney, liver, heart, lung, and pancreas) but does not cover corneas, eyes, or other tissues. Technically, all UNOS policies are voluntary; however, HRSA is currently developing regulations dealing with OPTN membership and operation.

Under a separate contract with HRSA, UNOS maintains a Scientific Registry for Transplant Recipients that includes information on all solid-organ transplant recipients (since October 1, 1987) from the date of transplantation until failure of the graft or death of the patient. In addition, HRSA informally conveys recommendations to organizations involved in procurement and transplantation of organs. Through OPTN and the Scientific Registry for Transplant Recipients, HRSA has the capacity to link organ donors and their recipients.

FDA regulates a limited number of specific tissues as either "biological products" or "medical devices." Examples of tissues include blood, dura mater, corneal lenses, umbilical veins, nonautologous cultured skin, and heart valves. In addition, FDA has recently published regulations regarding behavioral screening and infectious-disease testing (HIV-1, HIV-2, hepatitis B virus, and hepatitis C virus) for donors of human tissue for transplantation (14). FDA also regulates certain agents and devices for processing bone marrow, although bone marrow transplants from unrelated donors are under the auspices of NHLBI.

NHLBI manages the federal contract for the National Marrow Donor Program. Two bone marrow donor registries currently exist: one independent registry and one registry managed through the NHLBI contractor. Each registry group has voluntary guidelines/standards that resemble blood-banking standards. Although federal regulations have not yet been promulgated, the current practice of bone marrow acquisition and transplantation includes procedures to reduce the risk of HIV transmission. NHLBI is preparing regulations that will set forth criteria, standards, and procedures for entities involved in bone marrow collection, processing, and transplantation. These entities include the National Marrow Donor Registry, individual donor centers, donor registries, marrow-collection centers, and marrow-transplant centers. The regulations will include donor-selection criteria to prevent the transmission of infectious diseases, including HIV infection.

**Donor Screening**

PHS has made recommendations for preventing HIV transmission through organ/tissue transplantation and artificial insemination (1-3,15,16). These

recommendations include screening for behaviors that are associated with acquisition of HIV infection, a physical examination for signs and symptoms related to HIV infection, and laboratory screening for antibody to HIV.

PHS has made no specific recommendations for donation and banking of human milk, although HIV-infected women in the United States are advised to avoid breast feeding their infants because of the risk of HIV transmission through breast milk (17). The Human Milk Banking Association of North America has issued guidelines for the establishment and operation of human milk banks (18). These guidelines state that all human milk donors should be screened according to the American Association of Blood Banks' standards for screening blood donors. All milk accepted for donation should be pasteurized unless the recipient's condition requires fresh-frozen milk, in which case the milk bank director should consult with the medical director and advisory board to approve the dispensing of microbiologically screened, fresh-frozen milk from suitable donors.

Since March 1985, the FDA has licensed a number of screening and supplemental tests for detection and confirmation of HIV antibody. All these tests are intended for use on either fresh or freezer-stored samples of serum or plasma. The FDA has not required manufacturers to submit data showing that HIV-1 antigen and antibody-detection kits produce accurate results when applied to postmortem blood samples. Postmortem blood samples are often hemolyzed, which may affect the specificity of screening assays for HIV antibody (19,20).

The screening tests include enzyme immunoassays (EIAs), several of which are also approved for testing blood spots dried onto a specific filter paper, which may provide a method for storing samples. Rapid screening assays for HIV antibody that use a latex-agglutination or EIA (microparticle-based) format have also been approved for screening serum, plasma, or whole blood. A licensed EIA for detecting antibodies to HIV-2 is also commercially available, as are "combination tests" that simultaneously detect antibodies to HIV-1 and HIV-2 (21). FDA has also licensed one manufacturer to make and distribute a test for detection of HIV-1 p24 antigen for patient diagnosis and prognosis of HIV infection but not for screening blood donors.

Western blot tests and an immunofluorescence assay for HIV-1 are approved for supplemental, more specific testing of serum, plasma, and whole-blood samples found reactive by HIV-1 antibody screening tests. No additional, more specific test is approved that confirms either antibodies to HIV-2 (21) or eluted, dried blood-spot results. The licensed p24-antigen test includes a neutralization procedure that is to be used for specific testing of samples with repeatedly reactive test results.

Federal regulations already require that all donations of blood, blood components, and plasma intended for further processing into injectable products ("source plasma") be screened with a licensed test that detects HIV antibody. Since June 1992, PHS has also required that all blood and plasma donations be screened for HIV-2 antibody.

PHS has not recommended the use of the licensed HIV-1 p24-antigen assay for screening donated blood or source plasma, nor has the kit been approved for use in donor screening. This position is based on findings from several studies indicating that a blood donor with a positive test for antigen and a negative test for antibody is rare (22,23). Such rarity is probably attributable to the effectiveness of the donor-qualification procedures, including donor education, voluntary exclusion, and

antibody testing that together operate to prevent donation by persons at increased risk for HIV infection.

Limited studies have been conducted to examine the use of the p24-antigen assay to screen organ/tissue donors (19,20,24). Among approximately 1,000 samples from HIV-1 antibody-negative donors, no donors had detectable HIV-1 p24 antigen.

### ***Recipient Screening***

Until recently, PHS had made no recommendations regarding routine testing of recipients of organs, tissues, semen, or donated human milk. However, in response to the July 18, 1991, report of the PHS Workgroup on Organ and Tissue Transplantation, HRSA asked UNOS to request that transplant centers implement an interim voluntary HIV-testing policy for organ recipients. HRSA has requested that recipients be tested for HIV-1 antibody immediately before transplantation and at 3, 6, and 12 months after transplantation. If HIV infection is diagnosed in an organ recipient, the results of the HIV test are reported by the transplant center to the Scientific Registry for Transplant Recipients and to the procuring OPO, in accordance with existing state laws. No comparable registry exists for recipients of tissues, semen, or donated human milk. However, the National Marrow Donor Program routinely tracks both donors and recipients of bone marrow for unrelated-donor transplants. This program reports no known seroconversions among either donors or recipients, although recipients are not routinely screened for HIV.

Routine testing of recipients after transplantation has several potential benefits. First, early identification of HIV infection in a recipient allows for early intervention before signs and symptoms develop. Both antiviral therapy to prevent progression to acquired immunodeficiency syndrome (AIDS) (25) and prophylactic therapy to prevent opportunistic infections (26,27) have been recommended for HIV-infected patients, based on CD4+ T-lymphocyte levels. Second, early identification of HIV infection in a transplant recipient allows for early intervention to prevent further transmission from the recipient to sex or needle-sharing partners and to future offspring (through vertical transmission from mother to infant). Third, early identification of HIV infection in a recipient potentially identifies an infectious donor. Should further investigation indicate that the donor is the source of the HIV infection in the recipient, other recipients of tissue from that same donor can be notified and stored tissue can be retrieved, preventing further transmission through transplantation.

Concern has been expressed that linking HIV infection in a transplant recipient to the transplantation may be difficult because many recipients may have also received blood or blood products or have other risk factors. However, identification of multiple HIV-infected recipients of tissue from the same donor strongly implicates the donor as the source of the HIV infection in the recipients. In addition, stored blood or lymphoid samples from the donor (when available) can be tested for the presence of virus to confirm the HIV-infection status of the donor (4).

Questions have been raised about whether transplant recipients who may be receiving immunosuppressive therapy to prevent rejection are capable of producing antibody against HIV if transmission occurs. Several reports now indicate that the HIV-antibody response is not delayed in transplant recipients receiving antirejection therapy, which primarily affects cellular immunity (4).



The additional costs of routine screening for HIV in recipients must be considered as well. The Institute of Medicine has estimated that laboratory costs are approximately \$4 for a patient who tests negative and \$35 for a patient who tests positive. (The latter cost includes the added expense of repeat EIAs and Western blot or other supplemental tests.) These costs may be underestimates, however. The time required for pretest and posttest counseling was estimated to be approximately 0.5–1.0 hour for an HIV-seronegative patient and 1.5–2.0 hours for an HIV-seropositive patient (28).

#### **Inactivation of HIV in Tissues**

Thorough donor screening is considered the most effective method for preventing HIV transmission through transplantation; however, the use of chemical or physical inactivating or sterilizing agents to reduce further the already low risk of transmission has been considered. If such agents are to be useful, they must either inactivate or eliminate the virus while maintaining the functional integrity of the tissue or organ.

No mechanism for inactivating virus in whole organs currently exists. However, several agents have been suggested as possible disinfectants for tissues such as bone fragments (4). Pasteurization has been shown to inactivate HIV in human milk without substantially compromising nutritional and immunologic characteristics (29).

Although some physical and chemical agents have been shown to reduce the likelihood of isolating virus from treated solid tissues, conclusive evidence that those processes render solid tissue completely safe yet structurally intact is lacking. In the recent case of an HIV-infected donor who was antibody negative (4), tissues that had been processed in a variety of ways did not transmit HIV. These tissues included a) lyophilized fascia lata, tendons, or ligaments; b) dura mater that was lyophilized and irradiated with 3.0–3.4 Mrad of gamma radiation through a cobalt-60 source; c) bone fragments that were treated with ethanol and lyophilized; and d) one sample of fresh-frozen long bone with the marrow elements evacuated (4). However, because most of these tissues were relatively avascular, it is unclear whether the absence of HIV transmission was due to processing, avascularity, or both.

#### **General Considerations**

In developing guidelines for preventing HIV transmission from organ/tissue donors to recipients, several factors were considered: a) differences between the screening of living, brain-dead, and cadaveric donors; b) time constraints due to organ/tissue viability that may preclude performing certain screening procedures; c) differences in the risk for HIV transmission from various organs and tissues; d) differences between systems in place for procuring and distributing organs and tissues; e) the effect of screening practices on the limited availability of organs and some tissues; and f) the benefit of the transplant to the recipient (i.e., some transplants are lifesaving, whereas others are life enhancing).

Living donors can be interviewed about potential high-risk behavior, whereas deceased donors cannot. In the case of brain-dead or cadaveric donors, family members and others may be unable to provide an accurate risk history. Therefore, exclusion of potentially infected brain-dead or cadaveric donors relies even more heavily on laboratory screening and physical examinations than on interviews regarding high-risk behavior.

Screening procedures that require more than 24 hours to complete may not be feasible for brain-dead or cadaveric donors of organs and certain tissues. Most tissues must be recovered and most organs must be recovered and transplanted shortly after cessation of circulatory function of the donor. Whereas some tissues can be stored for months, others must be transplanted within a few days after procurement. These time constraints may limit the ability to interview certain family members or significant life partners who are not nearby and may preclude the use of certain laboratory screening tests that cannot be performed within these time constraints.

The precise risk of HIV transmission from various tissues is not known, yet some organs and tissues clearly present a higher risk for HIV transmission than others (4). For example, studies indicate that the risk for transmission from an organ of an HIV-infected donor is nearly 100%. Fresh-frozen, unprocessed bone also appears to carry a high risk for transmission, particularly if marrow elements and adherent tissue are not removed. Relatively avascular solid tissue, some of which is also processed by using techniques that might inactivate HIV, appears to carry a lower risk for HIV transmission.

As noted earlier in these guidelines, there is considerable variability in the role of federal agencies regarding transplantation of organs and tissues and the procurement and distribution systems. Oversight for, existence of, and compliance with recommendations also vary between these systems. When organs and tissues are procured from a single donor, tracking systems must involve multiple distribution systems that may be difficult to link.

Donor-screening practices must also consider the already inadequate supply of most organs and tissues needed for transplantation. However, even though attempts should be made to ensure the highest level of safety, donor-screening practices should not unnecessarily exclude acceptable potential donors.

Those involved in developing guidelines should consider that some transplants are lifesaving (e.g., a heart transplant), whereas others are life enhancing. Some physicians may be willing to offer the patient a transplant of a lifesaving organ from a donor whose HIV risk status is questionable but would not use life-enhancing tissue from such a donor.

## **RECOMMENDATIONS**

### **Donor Screening**

1. All prospective living donors or next of kin or significant life partners accompanying brain-dead or cadaveric donors should be informed of the general nature of the donor-evaluation process, including a review of medical and behavioral history, physical examination, and blood tests to exclude infectious agents that might be transmitted by organ or tissue transplant.
2. Prospective living donors or next of kin or significant life partners accompanying brain-dead or cadaveric donors should be informed about modes of transmission and risk factors for HIV infection, emphasizing that HIV can be transmitted via transplanted organs and tissues. They should be told that a negative test for HIV antibody does not guarantee that the donor is free of HIV infection because of the

rare situation of donation after infection but before seroconversion. Therefore, organs and tissue must not be transplanted from persons who may have engaged in activities that placed them at increased risk for HIV infection. This information should be presented in simple language to ensure that the donor, next of kin, or significant life partner understands what is considered high-risk behavior and the importance of excluding persons who have engaged in this behavior. Persons soliciting the donation should not place undue pressure to donate on potential living donors and those persons providing permission for potential brain-dead or cadaveric donors who might otherwise decline to donate or give permission because of high-risk behavior.

3. To ascertain risk factors, all prospective living donors should be interviewed in a confidential and sensitive manner by a health-care professional competent to elicit information about behaviors that place persons at risk for HIV infection. Interviewers should ask direct questions about high-risk behavior.
4. For potential pediatric donors for whom maternal transmission of HIV is a consideration, the mother and, if possible, the father should be interviewed about behaviors that may have placed them at risk for acquiring HIV infection that could have been transmitted to their child.
5. Except where retrieval occurs by legal authorization, the next of kin or significant life partner of brain-dead or cadaveric donors should be interviewed in a confidential and sensitive manner by a health-care professional regarding potential HIV risk factors in the donor. Other family members, friends, and sex partners may also need to be interviewed, if available. When consent for removal of organs/tissue is required, at least the person signing the consent form should be interviewed. Other possible sources of information about behavioral risk factors may include hospital, police, and coroner's records, if available. When an interview is not performed, as allowed by legal authorization, the transplant surgeon should be fully informed that the donation was accepted, even though a direct interview with the next of kin or significant life partner was not performed.
6. If available, the medical records, including autopsy reports of all donors, should be reviewed for signs and symptoms associated with HIV infection and for evidence of high-risk behavior (e.g., male-to-male sexual contact, acquisition of sexually transmitted diseases, exchange of sex for money or drugs, injecting-drug use, or birth to a mother either at risk for or infected with HIV).
7. All prospective donors of organs, solid tissue, and semen should undergo a physical examination as close as possible before donation, with special attention to physical signs of HIV disease and injecting-drug use. The extent of the physical examination should be determined by the responsible medical officials according to the context of organ/tissue donation. Human milk banks should obtain a release from the primary health-care provider certifying that the prospective donor is in good health and does not constitute a risk to potential recipients.
8. As with donors of blood and plasma, prospective living organ, tissue, semen, and milk donors found after careful screening to be acceptable donors should sign

a consent statement indicating that they have reviewed and understand the information provided regarding the spread of HIV and have agreed not to donate should they be at potential risk for spreading HIV. The statement should also indicate that prospective donors understand that they must be tested for HIV as part of the donor-screening process and will be notified of positive results as specified by any existing state statutes, regulations, or guidelines. For acceptable brain-dead or cadaveric donors, procurement personnel should document that a careful attempt has been made to eliminate persons at high risk through available information, including interview of family members or significant life partners, physical examination, review of medical records, autopsy findings, and any other records that might provide information about high-risk behavior or possible HIV infection. For either type of donor, the statement should be included as part of a general checklist or donor evaluation form covering all important aspects of the donor evaluation and should be included in the transplant records or record of the procuring agency. All records generated by the interview should be kept confidential.

#### **Donor Testing**

1. For all prospective donors, a blood sample obtained before any transfusions were administered (during the current hospital admission for inpatients) should be collected as close to the time of retrieval of tissue as possible. Bone marrow donors must provide blood samples far enough in advance of marrow harvest to permit the tests to be performed and results reported before the recipient's preparative regimen (marrow ablation) is begun. Samples should be tested for antibodies to both HIV-1 and HIV-2 by using FDA-licensed tests. Separate tests or a combination test for HIV-1 and HIV-2 may be used. All antibody-screening tests should be performed by EIA unless the condition of the recipient or donor dictates the use of a more rapid screening assay.
2. Transfusions and infusion of other fluids to the prospective donor might produce false-negative results because of hemodilution. Efforts should be made to perform HIV-antibody testing on the most recent pretransfusion/infusion specimen for which identity and quality can be ensured. Specimens should not be drawn immediately downstream from an intravenous site to prevent dilution with intravenous fluids.

Posttransfusion/infusion specimens may be considered for testing after efforts to obtain a pretransfusion/infusion sample have been exhausted and posttransfusion/infusion samples have been assessed for evidence of dilution. The suitability of posttransfusion/infusion samples must consider a) the volume of the material transfused as a percentage of the patient's total blood volume and b) the amount of time between the last transfusion/infusion and the collection of the sample to be tested. An exchange of one total blood volume will reduce the concentration of an intravascular substance such as IgG to 35% of initial levels if there is no replacement from the extravascular space. More than 50% of total body IgG is extravascular, and reequilibration to normal levels of IgG should be nearly complete within 24 hours of a total blood volume exchange of albumin (30).

3. The HIV p24-antigen assay may identify a few of the rare donors who are HIV-infected, yet antibody-negative; however, studies examining the utility of this assay for screening organ/tissue donors are limited and currently do not allow a definitive recommendation on the use of this test ( 19,24 ). The utility of other assays such as PCR, which are currently experimental, should be considered for evaluation as they become available for clinical use. Those institutions choosing to use the HIV-1 p24-antigen assay should be aware that in populations with low prevalence (e.g., organ/tissue donors), a large percentage of persons who test repeatedly reactive (without confirmation with the neutralization assay) will be false positive. Consideration should also be given to the potential problems with decreased specificity when the assay is used to test postmortem samples ( 19 ).
4. The testing algorithm for HIV-antibody assays should be performed as described in the package insert with an initial test and, if reactive, a retest on the same specimen. However, the time constraints of some situations may not accommodate the delay of repeat testing by EIA as described in the package insert. In such extreme cases of lifesaving organ transplantation, the sample should be set up in triplicate in the initial EIA. A repeatedly reactive result (positive screening test) is defined as reactivity above the test cutoff in two or more of the three assays. When testing by EIA is impractical, a more rapid licensed test should be performed in triplicate. Testing by the conventional algorithm should be performed as early as possible, even if it follows the procurement and/or transplant of the organs or tissues.
5. Results of HIV testing for organ/tissue donors should be handled confidentially, in accordance with general medical practices and applicable federal and state statutes, regulations, and guidelines.
6. Prospective living donors should be notified if they are found through the screening process to be HIV infected. Because of the possibility of sexual or parenteral transmission, the spouse or known sex partners of brain-dead or cadaveric donors should be notified in accordance with state law. All notifications should be handled in a manner congruent with current recommendations regarding counseling, testing, and partner notification ( 31,32 ). Before the notification of these persons, transplant and procurement organizations should consult with their state health department concerning local notification policies.

Also before notification, the repeatedly reactive screening assay should be confirmed with more specific supplemental tests. An aliquot of the original sample should be analyzed by using the following, more specific tests. For repeatedly reactive HIV-1 antibody EIAs, an HIV-1 Western blot or immunofluorescence assay should be performed. For repeatedly reactive HIV-1 antigen assays (if performed), a neutralization procedure must be performed. For HIV-2, no licensed supplemental test is available; however, consideration may be given to the use of research assays such as Western blot, immunofluorescence, radioimmune precipitation, and synthetic peptide-based EIA. Arrangements for HIV-2 supplemental testing may need to be made with either the state or local health department. For repeatedly reactive combination HIV-1 and HIV-2 assays, the published testing algorithm should be followed ( 21 ). When the results of any supplemental tests are unclear, the use of research assays should be considered.

Notification of HIV-infected prospective living donors or spouses/known sex partners of cadaveric donors should be done in accordance with state law and in a confidential and sensitive manner by staff competent in counseling and discussing positive HIV results and their implications. If such staff are not available in the organ/tissue procurement organization, arrangements should be made with other organizations such as health departments or clinics to provide appropriate notification.

7. When it is possible to properly obtain and store samples, one or more of the following samples from the donor should be saved for at least 5 years after the expiration date of the tissue: dried blood spots, a frozen buffy coat, spleen cells, lymph node cells, bone marrow, and an aliquot of serum. These samples can be examined if subsequent information indicates that the donor may have donated during the period after infection but before antibody seroconversion.
8. Confirmed positive HIV test results in a prospective organ/tissue donor should be reported to state health agencies if required by state law or regulation.

#### **Donor Exclusion Criteria**

Regardless of their HIV antibody test results, persons who meet any of the criteria listed below should be excluded from donation of organs or tissues unless the risk to the recipient of not performing the transplant is deemed to be greater than the risk of HIV transmission and disease (e.g., emergent, life-threatening illness requiring transplantation when no other organs/tissues are available and no other lifesaving therapies exist). In such a case, informed consent regarding the possibility of HIV transmission should be obtained from the recipient.

#### ***Behavior/History Exclusionary Criteria***

1. Men who have had sex with another man in the preceding 5 years.
2. Persons who report nonmedical intravenous, intramuscular, or subcutaneous injection of drugs in the preceding 5 years.
3. Persons with hemophilia or related clotting disorders who have received human-derived clotting factor concentrates
4. Men and women who have engaged in sex in exchange for money or drugs in the preceding 5 years.
5. Persons who have had sex in the preceding 12 months with any person described in items 1–4 above or with a person known or suspected to have HIV infection.
6. Persons who have been exposed in the preceding 12 months to known or suspected HIV-infected blood through percutaneous inoculation or through contact with an open wound, nonintact skin, or mucous membrane.
7. Inmates of correctional systems. (This exclusion is to address issues such as difficulties with informed consent and increased prevalence of HIV in this population.)

***Specific Exclusionary Criteria for Pediatric Donors***

1. Children meeting any of the exclusionary criteria listed above for adults should not be accepted as donors.
2. Children born to mothers with HIV infection or mothers who meet the behavioral or laboratory exclusionary criteria for adult donors (regardless of their HIV status) should not be accepted as donors unless HIV infection can be definitely excluded in the child as follows:

Children >18 months of age who are born to mothers with or at risk for HIV infection, who have not been breast fed within the last 12 months, and whose HIV antibody tests, physical examination, and review of medical records do not indicate evidence of HIV infection can be accepted as donors.

3. Children ≤18 months of age who are born to mothers with or at risk for HIV infection or who have been breast fed within the past 12 months should not be accepted as donors regardless of their HIV test results.

***Laboratory and Other Medical Exclusionary Criteria***

1. Persons who cannot be tested for HIV infection because of refusal, inadequate blood samples (e.g., hemodilution that could result in false-negative tests), or any other reasons.
2. Persons with a repeatedly reactive screening assay for HIV-1 or HIV-2 antibody regardless of the results of supplemental assays.
3. Persons whose history, physical examination, medical records, or autopsy reports reveal other evidence of HIV infection or high-risk behavior, such as a diagnosis of AIDS, unexplained weight loss, night sweats, blue or purple spots on the skin or mucous membranes typical of Kaposi's sarcoma, unexplained lymphadenopathy lasting >1 month, unexplained temperature >100.5 F (38.6 C) for >10 days, unexplained persistent cough and shortness of breath, opportunistic infections, unexplained persistent diarrhea, male-to-male sexual contact, sexually transmitted diseases, or needle tracks or other signs of parenteral drug abuse.

***Inactivation of HIV in Organs/Tissues***

Definitive recommendations cannot yet be made regarding inactivation of HIV in organs and tissues because of lack of information about potentially effective inactivation measures. Research should continue in this area. Efforts to evaluate the effect of certain processing techniques on tissue sterility and quality should be expanded to include virologic studies for HIV. Thus, until more is known, it is prudent to process bone and bone fragments and carefully evacuate all marrow components from whole bone whenever feasible.

***Quarantine***

For semen donations and, when possible, for tissue donations from living donors, the collection should be placed in frozen quarantine and the donor retested for

antibodies to HIV-1 and HIV-2 after 6 months ( 15 ). The quarantined material should be released only if the follow-up test results have been obtained and are negative.

#### **Record Keeping for Tracking of Recipients and Tissues**

1. Each establishment involved in the acquisition, processing, distribution, or storage of organs or tissues should have a graft identification system that allows the tracking of organs and tissues from the donor source to the recipient institution and vice versa. Furthermore, each establishment involved in the acquisition of organs or tissues from a single donor should have mechanisms in place to facilitate the communication between establishments for the purposes of tracking organs and tissues to recipients who should be notified if HIV transmission from donor source material is confirmed. Procurement, processing, distribution, and storage centers should keep accurate records of the distribution of each organ/tissue according to the donor identification number, tissue type and identifying number, and identifying information for the receiving center, along with dates of procurement and distribution. Records should be kept a minimum of 10 years after expiration of tissue.
2. The transplantation center, hospital, physician, or dentist should keep accurate records of all organs/tissues received and the disposition of each. These records must be separate from patients' medical records (e.g., in a log book) so that this information is easily obtainable should tracking be necessary. Recorded information should include the organ/tissue type; donor identification number; name of procurement or distribution center supplying the organ/tissue; recipient-identifying information; name of recipient's physician or dentist; and dates of a) receipt by the center and b) either transplantation to the recipient or further distribution.
3. The donor identification number and organ or tissue type should be recorded in the recipient's transplant/medical/dental record.

#### **Testing and Reporting of Recipients**

1. Health-care providers for transplant recipients and the recipients themselves should be aware of the small but potential risk of infections, including HIV, from transplanted organs and tissues. The recipient's informed consent to the transplant should include acknowledgment of the risks, including transmission of HIV and other infections.
2. Until the risk for HIV transmission from screened donors has been clarified, recipients of solid organs should be routinely advised to be tested for HIV immediately before transplantation and at 3 months following the transplant. Testing of recipients should be done with consent of the recipient and should not be mandatory. Recipients of tissues other than solid organs do not require routine testing for HIV following receipt of the tissue from appropriately screened donors. Results of HIV testing of organ recipients should be collected and analyzed by the Scientific Registry for Transplant Recipients. (If data indicate no benefit from recipient testing, then this recommendation for recipient testing may be omitted in a revision of these guidelines.)



3. If a transplant recipient is found to be infected with HIV, the transplant center or health-care provider should, consistent with state law, immediately notify the state health department and the organization from which the tissue was obtained. HIV infection in a solid-organ recipient should also be reported to the Scientific Registry for Transplant Recipients.

#### **Recall of Stored Tissue and Tracking of Recipients of Organs/Tissue from HIV-Infected Donors**

1. Upon being notified that an organ/tissue recipient is infected with HIV, the organ/tissue collection center, in collaboration with the state or local health department and with assistance from CDC, is responsible for determining as soon as possible whether the donor was HIV-infected. This is done by determining the HIV-infection status of other recipients of organs/tissues (particularly those recipients of organs and fresh-frozen bone) and by laboratory testing of stored donor material. Experimental diagnostic laboratory assays such as PCR may be useful in these situations and should be used when they become available.
2. If evidence suggests HIV infection in the donor either from testing of stored donor specimens or by finding HIV infection in other recipients, all other recipients of that donor's tissue or organs should be notified through their transplanting physician and informed of the likelihood of HIV exposure and advised to undergo HIV testing.
3. HIV-infected recipients should be counseled about their need for medical evaluation and about prevention of HIV transmission to others. They should also be advised to inform their sex or needle-sharing partners of their potential risk and need for HIV counseling and testing. HIV-infected women should be informed of the risk of transmission of HIV to their children born after the transplant and be advised to have these children evaluated and to avoid breast-feeding. Pregnant women should receive pregnancy counseling about HIV.
4. All stored organs/tissues from a donor found to be HIV-infected should be retrieved and quarantined immediately and either used only for research purposes or destroyed, except when the transplantation of an indispensable organ/tissue is necessary to save the patient's life.

[61 FR 19745, May 2, 1996]

## **PART 488—SURVEY, CERTIFICATION, AND ENFORCEMENT PROCEDURES**

### **Subpart A—General Provisions**

#### **Sec.**

- 488.1 Definitions.
- 488.2 Statutory basis.
- 488.3 Conditions of participation; conditions for coverage; and long-term care requirements.
- 488.4 Application and reapplication procedures for accreditation organizations.
- 488.5 Effect of JCAHO or AOA accreditation of hospitals.

488.6 Other national accreditation programs for hospitals and other providers and suppliers.

488.7 Validation survey.

488.8 Federal review of accreditation organizations.

488.9 Onsite observation of accreditation organization operations.

488.10 State survey agency review: Statutory provisions.

488.11 State survey agency functions.

488.12 Effect of survey agency certification.

488.14 Effect of PRO review.

488.18 Documentation of findings.

488.20 Periodic review of compliance and approval.

488.24 Certification of noncompliance.

488.26 Determining compliance.